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Case Report
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Treatment of recurrent pulmonary thromboembolism with echosonic endovascular system

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ABSTRACT

Venous thromboembolism is a collective term that describes two diseases, pulmonary thromboembolism (PE) and deep vein thrombosis, with or without symptoms but often accompanying each other. PE develops in most cases due to thrombus formation in the deep veins of the lower extremities and migrates to the pulmonary artery and/or its branches. It is a preventable disease with high mortality and morbidity and includes diagnostic difficulties. Recurrence may occur despite treatment in 5-23% of PE cases. Patients may apply to the hospital with symptoms such as unexplained dyspnea, stabbing or atypical chest pain, hemoptysis, and syncope. We aimed to present the patient who had chronic deep vein thrombosis (DVT) and was frequently hospitalized due to recurrent massive PE. In our case, disease status requires catheter thrombolytic therapies two times in three months.

Keywords: Venous thromboembolism, massif pulmonary thromboembolism, ecosonic endovascular system

INTRODUCTION

Venous thromboembolism is a collective term that describes two diseases, pulmonary thromboembolism (PE) and deep vein thrombosis, with or without symptoms but often accompanying each other. PE develops in most cases due to thrombus formation in the deep veins of the lower extremities and migrates to the pulmonary artery and/or its branches.

The major risk factors are fracture in lower extremity, heart failure or atrial fibrillation/flutter, hospitalization due to (in the last 3 months), hip or knee replacement, major trauma, myocardial infarction in the last 3 months, previous VTE and, spinal cord injury. The medium risk factors are arthroscopic knee surgery, autoimmune diseases, blood transfusion, central venous catheter, intravenous catheters, chemotherapy, congestive heart failure or respiratory failure, erythropoiesis stimulating agents, hormone replacement therapy, in vitro fertilization, oral contraceptive therapy, postpartum treatment, infection (especially pneumonia, urinary tract infection and HIV), inflammatory bowel disease, cancer (risk is high in the presence of metastasis), paralytic stroke, superficial vein thrombosis, and thrombophilia. The weak risk factors are bed rest for more than three days, diabetes mellitus, arterial hypertension, sitting still for long periods of time (plane or car travel), advanced age, laparoscopic surgery (cholecystectomy), obesity, pregnancy, varicose veins, and venous catheters.

It is a preventable disease with high mortality and morbidity and includes diagnostic difficulties. Recurrence may occur despite treatment in 5-23% of PE cases.[1] Patients are typically admits to the hospital with symptoms such as unexplained dyspnea, stabbing or atypical chest pain, hemoptysis, and syncope. We aimed to present the patient who had chronic deep vein thrombosis (DVT) and was frequently hospitalized due to recurrent massive PE. In our case, disease status requires catheter thrombolytic therapies two times in three months.

CASE

A 44-year-old female patient was consulted to us by a gynecologist and obstetrician due to shortness of breath, stabbing chest pain and low oxygen saturation that developed after endometrium curettage biopsy. It was learned that she had known hyperthyroidism and chronic DVT. The patient developed a pulmonary embolism about a year ago and had a vascular surgery while a temporary vena cava filter was installed during the surgery. The patient was given on rivaroxaban 20 mg 1x1. The patient had stopped rivaroxaban treatment about 2 weeks ago due to vaginal bleeding. She had no history of additional pulmonary disease. She had never smoked. She had no known family history of cardiopulmonary disease. She had known no history of

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malignancy in her family or herself. She is a housewife and had no jobs but the whole family is farmer and she contributes to the family business. There was no recurrent pregnancy loss. During physical examination, breathing sounds were normal on auscultation. While pulse oxymeter was 97% at rest, the saturation was 73% after a 6-minute exercise test. Respiratory rate was 26/min, pulse 102/min, blood pressure 110/70 mmHg. In arterial blood gas, pH: 7.38 pCO_2: 33.7 pO_2: 72.6. Sinus tachycardia was detected in electrocardiography. On echocardiography, the right heart chambers were evaluated as normal and systolic pulmonary arterial pressure (sPAP) was evaluated as 30 mmHg. Laboratory tests resulted in D-Dimer level of 3530 ng/ml. Renal function tests and infection parameters were normal. An iso-hyperechoic thrombus was observed within the vein lumen in lower extremity venous Doppler ultrasonography.

In the patient's computed tomography (CT) pulmonary angiography, a filling defect compatible with embolism was observed in the lobar and segmental branches of the right pulmonary artery (Figure 1-4). The patient was diagnosed with massive PE. Enoxaparin sodium 2x0.6 ml subcutaneous was given during hospitalization. The rheumatologic markers, tumor markers and genetic evaluation of thrombophilia panel were found to be normal. The patient, who showed a clear improvement after the treatment, was discharged by continuing the rivaroxaban 20 mg/day.

Figure 1. There was a massive trombus in right main pulmonary artery

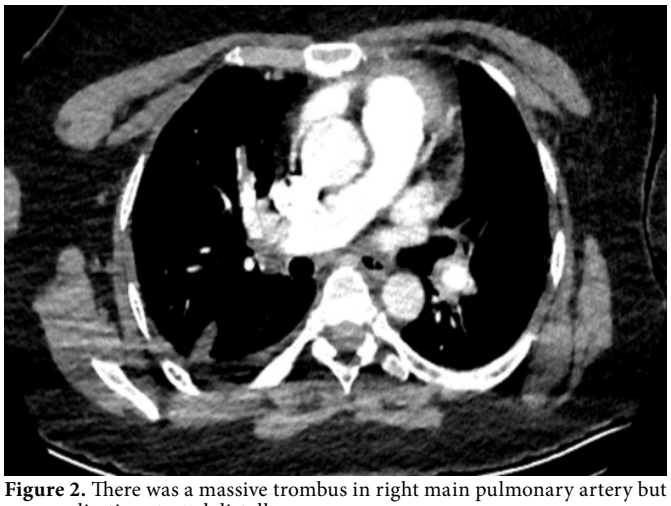

Figure 2. There was a massive trombus in right main pulmonary artery but a recanalisation started distally

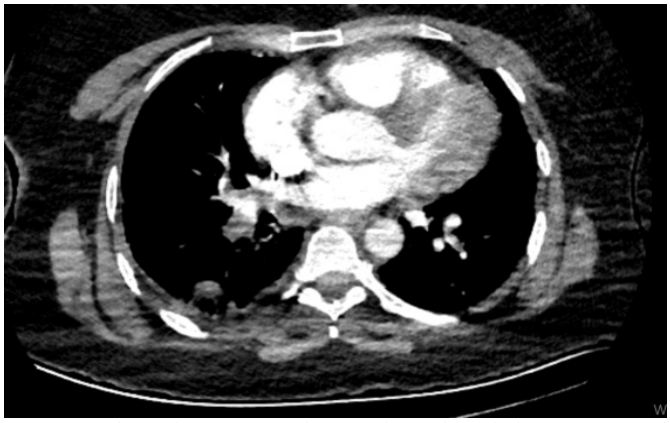

Figure 3. The right atrium and ventricle is dilated due to increased pulmonary hypertension

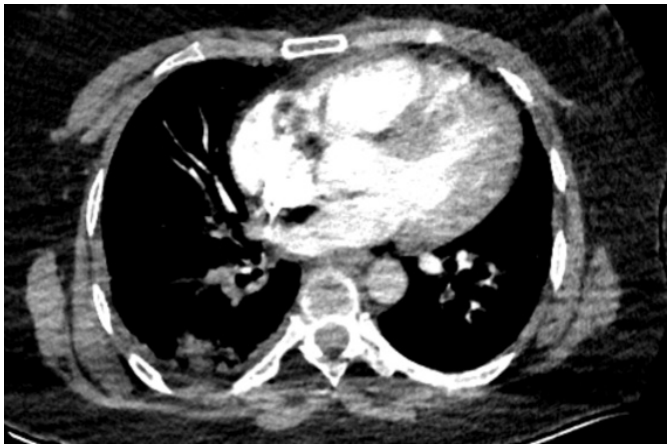

Figure 4. There is a necrosis area at the right lower lob posterior segment

The patient was admitted to the emergency room two months later with similar complaints and was hospitalized again. In current laboratory tests, D-Dimer was 1480 ng/ml and CT pulmonary angiography was reported as "hypo dense linear septations and incomplete thrombosis appearances compatible with right pulmonary artery, lower lobe segmental and left main pulmonary artery lower lobe segmentary-subsegmental chronic PE were observed." While the patient's treatment was continuing, the patient was consulted to cardiovascular surgery. The patients and relatives consent was taken for thrombolytic therapy. In the angiography unit, thrombolytic infusion was applied directly on the thrombus by reaching the pulmonary artery from the femoral vein with the Echosonic Endovascular System (EKOS) catheter, which is an ultrasound-accelerated thrombolytic treatment method, for a period of 24 to 48 hours (Figure 5-6). As thrombolytic therapy, alteplase 50 mg 1x1 was used intravenously for two days. After the EKOS procedure, heparin 25.000 IU was administered intravenously for two days in the intensive care unit. Oxygen saturation remained stable at rest. She discharged to the ward and after a successful 6-minute exercise test, she was discharged with medical therapy while sPAP was 30 mmHg.

The patient re-admitted to the emergency department 3 months later with severe shortness of breath and chest pain. The patient's current CT pulmonary angiography showed "hypodense thrombus was observed in the left main pulmonary artery, and a hypo dense thrombus area was also observed in the lower lobe branch of the right pulmonary artery. A wedge-shaped infarct area with its base resting on the pleura was observed in the laterobasal segment of the

lower lobe of the right lung. Similarly, there are infarct areas in the posterobasal segment of the upper lobe of the left lung, with a necrotic component and a base resting on the pleura." Echocardiography showed that the right heart chambers were wide, EF: 60%, systolic PAP: 80 mmHg. The patient was hospitalized, her treatment started with low molecular weight heparin (LMWH), and she was consulted again to cardiovascular surgery. It was decided to give the patient thrombolytic via catheter again, and the patient underwent an interventional procedure with the EKOS catheter again. The hemoglobin, hematocrit and platelet values before and after the procedure were normal. The thrombolytic procedure was successful again and the patient, whose "international normalized ratio" (INR) was monitored, was started on warfarin sodium 5 mg tablet and the dose was reduced and switched to 2.5 mg tablet. The follow-up of the patient continued without any problems, and systolic PAP decreased to 40 mmHg in the post-intervention echocardiography. The patient was taken to the pulmonary rehabilitation program at the hospital and discharged with full recovery. The patient's follow-up is still being carried out closely for chronic thromboembolic pulmonary hypertension (CTPH).

Figure 5. The catheterisation of right pulmonary artery

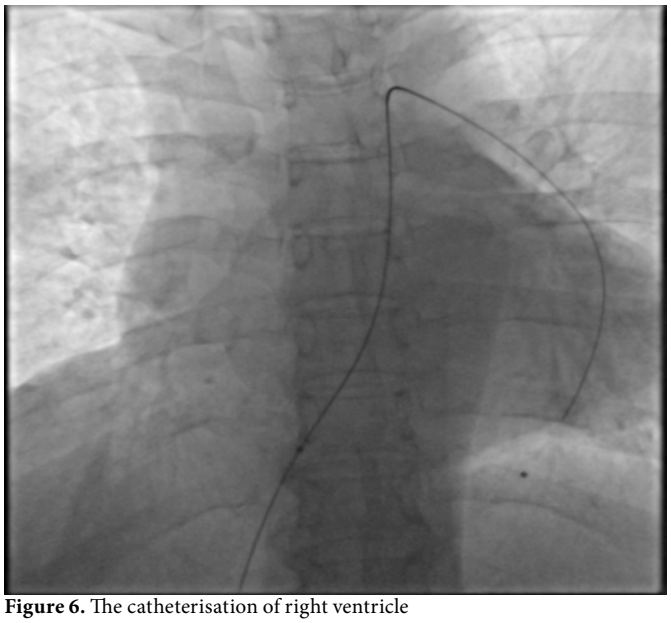

Figure 6. The catheterisation of right ventricle

DISCUSSION

This case was a recurrent PE and threated two times with thrombolytic therapy. The patient is a young woman and had no reason for thrombophilia. The genetic evaluation was also normal. There was not any provoked PE or VE. We searched the patient for any malignancy or infection and found nothing until today. The patient is relieved after the last thrombolytic therapy and she was given warfarin.

PE is a disease with high complications, morbidity and mortality. In cases of venous thromboembolism, recurrence may occur under treatment and after treatment is completed. Recurrence rates under treatment were varying between 0.6% and 2.5%. Especially in the first two years after venous thromboembolism (VE), the risk of recurrence is highest. Afterwards, the risk continues to decrease. VE recurrence increases the risk of mortality. Many risk factors have been identified that increase susceptibility to venous thromboembolism. The most frequently reported risk factors in studies are; previous history of VE, active cancer, major trauma, surgery, recent hospitalization, long flights, immobility, obesity and accompanying heart diseases.[2] These risk factors are thought to increase intravascular coagulation, leading to venous thromboembolism. Factors causing intravascular clotting; it was defined by Virchow in 1856 as "1. vascular endothelial damage 2. hypercoagulability 3. stasis". In 75% of VE cases, acquired and/or hereditary factors causing one of these three factors are detected.[3] In PE, a series of pathophysiological events are triggered by the settling of the thrombus in the lungs. The number and diameter of the occluded vessels, the size of the embolism, the patient's cardiopulmonary reserve, reflex vasoconstriction due to pulmonary artery dilation, inflammatory mediators, vasoconstriction due to serotonin, thromboxane and fibrinogen degradation product fibropeptide B secreted from platelets affect the pathophysiological events and clinical findings in PE.[4,5]

Correct treatment of the disease is as important as diagnosing it. Pulmonary thromboembolism has a high clinical suspicion and moderate clinical probability, and anticoagulant therapy should be initiated in patients with a low risk of bleeding while awaiting test results.

Once the diagnosis is confirmed, LMWH or standard heparin (SH) should be started. This treatment should be continued for at least five days. Oral anticoagulant is added to the treatment within the first 24 hours. In those with low bleeding risk, giving 10 mg warfarin in the first two days allows the INR value to reach ≥2 more quickly, thus shortening the hospital stay. It is recommended to start warfarin treatment at a dose of 5 mg/day in patients with bleeding risk and in elderly patients (>75 years of age). When the INR value is found to be between 2.0-3.0 for two consecutive days, heparin is discontinued and treatment is continued with oral anticoagulant only for at least three months. Initial treatment is three weeks for rivaroxaban and seven days for apixaban. If the patient's initial treatment was with an oral direct factor Xa inhibitor (rivaroxaban or apixaban), maintenance treatment is continued with the maintenance dose of the same drug. Oral direct thrombin inhibitor (dabigatran) or direct factor Xa inhibitor (edoxaban) can also be used instead of warfarin in maintenance treatment.[6]

Reperfusion therapy can be lifesaving in cases with high mortality risk. Systemic thrombolytic therapy is the most commonly used treatment for reperfusion purposes. In recent years, interventional treatments with percutaneous catheters have begun to be used with increasing frequency. In cases where neither can be used or are not effective, the only option is surgical embolectomy. In cases of pulmonary thromboembolism, thrombolytic drugs, which actively dissolve the thrombus, provide rapid improvement in pulmonary perfusion, hemodynamics, and gas exchange and right ventricular functions. This improvement is most evident when given within the first 48 hours of the onset of symptoms, but has also been shown to be beneficial when given within 14 days. Clinical improvement with thrombolytic therapy in patients with high mortality risk and right ventricular recovery demonstrated by transthoracic echocardiography (TTE) after 36 hours have been demonstrated in 98% of patients given thrombolysis.[7,8] In patients with moderate-high risk PTE who cannot receive thrombolytic treatment due to the risk of bleeding, who cannot respond to thrombolytic treatment, or whose critical condition does not allow waiting for the effective time of systemic thrombolytic treatment, or who have a tendency to hemodynamic deterioration, selected massive (high risk) PE can be treated with a percutaneous catheter if sufficient experience is available. Reperfusion therapy can be tried by performing interventional treatment.[9] The aim of catheter-based interventions is to quickly reduce pulmonary artery pressure, right ventricular load and pulmonary vascular resistance, increase systemic perfusion and improve right ventricular functions. Intrapulmonary thrombolytic therapy has no advantage over systemic administration. With thrombolytic therapy, the obstruction in pulmonary blood flow in the early stages of acute PE is rapidly eliminated, lung blood supply is restored, sPAP decreases, and thus cardiogenic shock is prevented. Agents such as streptokinase, urokinase, alteplase and tissue plasminogen activator (tPA) are used as thrombolytic agents. However, in catheter-guided thrombolytic treatments, tPA is used more frequently due to the low incidence of side effects and rapid onset of action.[10]

CONCLUSION

In case of recurrent thromboembolism, especially in massive PE cases that develop due to choronic DVT, as in our patient, percutaneous intravascular thrombolytic therapy should be considered as an alternative to systemic thrombolytic therapy and patients should also be evaluated in terms of thrombolytic treatment with EKOS.

ETHICAL DECLARATIONS

Informed Consent

The patient signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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